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Sustained low-efficiency dialysis for critically ill patients requiring renal replacement therapy

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Background. The replacement of renal function for critically ill patients is procedurally complex and expensive, and none of the available techniques have proven superiority in terms of benefit to patient mortality. In hemodynamically unstable or severely catabolic patients, however, the continuous therapies have practical and theoretical advantages when compared with conventional intermittent hemodialysis (IHD).

Methods. We present a single center experience accumulated over 18 months since July 1998 with a hybrid technique named sustained low-efficiency dialysis (SLED), in which standard IHD equipment was used with reduced dialysate and blood flow rates. Twelve-hour treatments were performed nocturnally, allowing unrestricted access to the patient for daytime procedures and tests.

Results. One hundred forty-five SLED treatments were performed in 37 critically ill patients in whom IHD had failed or been withheld. The overall mean SLED treatment duration was 10.4 hours because 51 SLED treatments were prematurely discontinued. Of these discontinuations, 11 were for intractable hypotension, and the majority of the remainder was for extracorporeal blood circuit clotting. Hemodynamic stability was maintained during most SLED treatments, allowing the achievement of prescribed ultrafiltration goals in most cases with an overall mean shortfall of only 240 mL per treatment. Direct dialysis quantification in nine patients showed a mean delivered double-pool Kt/V of 1.36 per (completed) treatment. Mean phosphate removal was 1.5 g per treatment. Mild hypophosphatemia and/or hypokalemia requiring supplementation were observed in 25 treatments. Observed hospital mortality was 62.2%, which was not significantly different from the expected mortality as determined from the APACHE II illness severity scoring system.

Conclusions. SLED is a viable alternative to traditional continuous renal replacement therapies for critically ill patients in whom IHD has failed or been withheld, although prospective studies directly comparing two modalities are required to define the exact role for SLED in this setting.

Key words: continuous veno-venous hemodialysis, acute renal failure, critical care medicine, intermittent hemodialysis, SLED, kidney failure.

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The extracorporeal replacement of renal function for critically ill patients is managed by the complementary techniques of conventional intermittent hemodialysis (IHD) and continuous renal replacement therapies (CRRTs). To date, neither technique has proven superiority in terms of benefit to patient mortality (abstract; Mehta et al, *J Am Soc Nephrol* 5:7, 1996) [1–3], and selection for a given patient is usually based on the clinical situation, clinician proficiency with the technique, and logistic capabilities of the institution and intensive care unit (ICU)/dialysis personnel [4, 5].

There are relative advantages and disadvantages to IHD and CRRTs. IHD is the more traditional technique and is familiar to most nephrologists and nursing personnel. Modern IHD machinery allows for precise volumetric ultrafiltration control and online bicarbonate dialysate production. IHD is rendered feasible by virtue of high intradialytic solute clearances, which allow for brief treatment times and easy access to patients for out-of-unit diagnostic and therapeutic procedures. However, the ultrafiltration of substantial fluid volumes over short treatment times is frequently associated with hemodynamic instability in critically ill patients, thus limiting the removal of obligatory fluid loads [6]. Ironically, despite high intradialytic solute clearances, the dose of dialysis delivered in acute renal failure (ARF) tends to be low compared with targets established for end-stage renal disease (ESRD; abstract; Jaber et al, *J Am Soc Nephrol* 8:284A, 1997) [7], and this may be relevant to patient outcome (abstract; Schiffl et al, *J Am Soc Nephrol* 8:290A, 1997) [8]. Furthermore, with IHD, solute control is periodic, and subsequent disequilibrium and water shifts may worsen brain edema and increase intracranial pressure [9].

Compared with IHD, there is better tolerance to ultrafiltration with CRRTs due to a slower rate of fluid re-

moval [3, 10–12] and improved steady-state azotemia control even for severely catabolic patients [13]. However, implementation of a CRRT program is expensive because of costs related to specialized machinery, filters and lines, and filtrate replacement fluid [10, 14]. Logistically, CRRTs may be unfamiliar to many nephrologists [15] and also result in increased workload for already busy intensive care nurses. CRRTs are frequently interrupted with out-of-unit diagnostic and therapeutic procedures, which leads to a reduction in dialysis dose from "down time," as well as the expense and inconvenience from unscheduled extracorporeal blood circuitry replacement [16]. Furthermore, there is a definite need for continuous anticoagulation during CRRTs to prevent extracorporeal blood circuit clotting [6].

Preliminary reports have emerged from several centers concerning hybrid techniques that utilize standard IHD equipment, but have therapeutic aims in common with CRRTs, that is, lower solute clearances maintained for prolonged periods of time (abstracts; Chatoth at al, *Blood Purif* 17:16, 1999; and Hu et al, *Blood Purif* 17:15, 1999) [17]. We hypothesized that the ideal renal replacement therapy for critically ill patients would be characterized by (*1*) adequate solute control, (*2*) precise achievement of ultrafiltration goals without hypotension, (*3*) satisfactory patient outcomes, (*4*) high acceptance by nursing personnel, (*5*) procedural simplicity and low cost, and (*6*) nocturnal scheduling allowing unrestricted patient access for daytime procedures and tests. These principles have provided the rationale for the development of a dialysis technique named sustained low-efficiency dialysis (SLED), which was introduced in July 1998 at the University of Arkansas for Medical Sciences (UAMS). We present here a detailed description of our experience accumulated over 18 months.

METHODS

Patient selection

All critically ill patients requiring renal replacement therapy were considered for SLED. Clinician determination defined the need for renal replacement therapy based on standard indications. SLED treatments were performed for patients in whom IHD (*1*) had repeatedly failed (therapy termination before 50% completion) due to intradialytic hypotension unresponsive to increased inotropic support and/or resuscitative fluid administration, (*2*) had been withheld because of clinician determination that hemodynamic intolerance was likely, and (*3*) had failed to achieve overall goals in solute control despite daily IHD.

Technical considerations

Default dialysate (Q_D) and blood flow (Q_B) rates were set at 100 and 200 mL/min, respectively. A 12-hour duration was prescribed to allow for gradual fluid removal, to provide good solute clearance based on animal experiments [18, 19], and to coincide with ICU nursing shifts.

The Fresenius 2008H [Fresenius Medical Care North America (FMC-NA), Lexington, MA, USA] was utilized without additional software or hardware with standard lines and F8 low flux polysulfone (FMC-NA) hemodialyzers. Angioaccess was established with central venous hemodialysis catheters. In the absence of contraindication, patients were systemically anticoagulated with unfractionated heparin to prevent extracorporeal blood circuit clotting. A loading dose of heparin was given at the initiation of a SLED treatment and/or an infusion (100 IU/mL) into the extracorporeal blood circuit proximal to the hemodialyzer. Heparinization was guided by serial measurement of the activated partial thromboplastin time (APTT), which was drawn peripherally and targeted to be 1.5 times control. Online dialysate was generated with a bicarbonate proportioning system using tap water treated with a reverse osmosis (RO) system. The Q_D of 100 mL/min allowed a canister of dialysate concentrate to last the entire treatment without replacement (maximum ≈17 hours). Dialysate composition was varied according to clinical needs, but the default dialysate contained $[K^+]$ of 4.0 mEq/L, $[HCO_3^-]$ of 35 mmol/L, and $[Ca^{2+}]$ of 2.5 mEq/L.

Minor adjustments were necessary to the operating parameters of the 2008H in a service mode. The Q_D of 100 mL/min required activation of the "slow dialysis" option. Prior to the initiation of SLED, recalibration of the temperature control to 37°C at a Q_D of 100 mL/min was necessary to avoid persistent low dialysate temperature alarms. Although not mandatory for the performance of SLED with the 2008H, new CRRT software is available that eliminates the need for recalibration and includes a dedicated screen for CRRT for a clearer interface with the nurse managing the treatment.

Logistic considerations

At the inception of the SLED program, treatments were deliberately scheduled during the day to allow ICU nurses to become familiar with the SLED procedure. In 1999, with the program firmly established, treatments were largely nocturnal (>75% of treatment start times between 1600 and 2400 h), reflecting the original rationale and intention for SLED.

The nephrology team assumed medical responsibility for SLED. Prescription and objectives of SLED were generally discussed and endorsed by both nephrology and the ICU medical staff. Interrupted treatments were sometimes re-initiated by the on-call dialysis nurse after consultation with the responsible nephrologist. Treatments could be discontinued at the discretion of the nephrologist if therapeutic objectives had been achieved by the time of the interruption. SLED continued to be utilized

until patients were hemodynamically stable enough to be managed with IHD. Generally, patients were treated with daily or alternate-day SLED according to clinical need.

Protocols were developed to establish operational procedures and to define relative responsibilities between the ICU and dialysis nursing personnel. The dialysis nurse educator was responsible for training all of the ICU nursing personnel. Dialysis nurses were responsible for the provision and initiation of SLED treatments, while troubleshooting and discontinuation responsibilities were shared. The ICU nurses performed hourly monitoring and documentation and management of machine alarms according to simple algorithms. The dialysis nurses were always available in house or from home for advice and assistance to the ICU nurse.

Evaluation of SLED

The study protocol was approved by the UAMS Human Research Advisory Committee, and informed consent was obtained from all patients in accordance with the guidelines proposed in the Declaration of Helsinki [20].

A single-center SLED registry was instituted in July 1998, and data were prospectively collected by MD investigators and entered into an Access-based (Microsoft Corporation, Seattle, WA, USA) relational database for future analysis. Patient data collection included demographic characteristics, primary and renal diagnoses, and outcomes. Treatment data collection included ultrafiltration volumes, patient vital signs, inotropic agent requirements, and details of SLED prescription. Complications noted by nursing or medical staff at the time of SLED were also reviewed and logged.

Illness severity was determined for each patient by the APACHE II scoring system [21]. The use of this system for outcome prediction was originally validated in prospective multicenter studies, utilizing scores that were calculated from physiological measurements at the time of ICU admission. More recently, the APACHE II scoring system also has been validated in a prospective multicenter fashion for patients specifically with ARF, but with scores determined at the time of dialysis initiation [22, 23]. Accordingly, two APACHE II scores were calculated for each patient in our cohort, the first from physiological variables obtained during the first 24 hours of ICU admission and the second from those obtained during the 24 hours before the initiation of dialytic treatment in the ICU. Expected hospital mortality rates for the APACHE II scores were calculated using the logistic regression calculations suggested in the original article to adjust for the initial admitting diagnosis. The predictive capacity of the APACHE II model in the SLED patient cohort (goodness-of-fit) was assessed by the Hosmer-Lemeshow statistic. This statistic measures the correspondence between the number of observed hospital deaths and the number of expected hospital deaths from the APACHE II model within each 10% stratum of the cohort's expected risk of death. Hospital mortality ratios and 95% confidence intervals (regarding observed mortality as a binomial variable) were obtained by dividing the observed by expected hospital mortality [24].

Unless otherwise stated, the results are expressed mean ± SD (range). Means were compared by the Student *t* test. All SLED patients and treatments were evaluated on an intention-to-treat basis.

Laboratory methods

Blood and dialysate solutes were monitored at two hourly intervals during a single SLED treatment in consenting patients. A blood sample was collected at one-hour post-SLED, at which time solute equilibrium was assumed (abstract; Lo et al, *J Am Soc Nephrol* 8:287A, 1997) [25]. Chemical analyses were performed in triplicate by multianalyzer (Dade Dimension Flex Clinical Chemistry Systems, Newark, DE, USA). Total dialysate collection was undertaken using serially arranged sterile 15 L peritoneal dialysis cycler effluent bags (Baxter Healthcare Corporation, Deerfield, IL, USA). Blood (from the hemodialysis catheter at $Q_B = 0$) and dialysate were collected by a single investigator (M.M.) at strictly timed intervals. All samples were immediately processed (blood) or immediately frozen at −70°F for later testing (dialysate). Plasma water was assumed to be 93% of plasma volume, and this factor was used to convert serum to plasma water concentrations for dialysate-based kinetic calculations. Dialysate phosphate determinations were performed in triplicate [Dade Dimension clinical chemistry system, intra-assay coefficient of variation (CV) 1.4%, inter-assay CV 3.6%] to estimate the total phosphate removal. Dialysate urea nitrogen determinations were performed in triplicate (Dade Dimension Clinical Chemistry System; intra-assay CV 2.6%, interassay CV 4.8%) to estimate the total urea nitrogen removal, and double-pool Kt/V using urea kinetic models (UKM) based on dialysate collection theory (**Appendix**) [26].

RESULTS

Patient characteristics

Sustained low-efficiency dialysis treatments were performed in 37 patients whose clinical profiles are provided in Table 1. Median age was 58 years. Five patients were primarily managed by the cardiovascular service, 6 by surgery, and 21 by internal medicine. Eighteen patients did not have a history of underlying renal disease, whereas 19 had chronic renal impairment with a baseline serum creatinine value >1.4 mg/dL. Four of these had ESRD. Fifty-one SLED treatments were performed in patients while they were anuric. In the remainder, urine

Table 1. Clinical characteristics of 37 patients treated with sustained low efficiency dialysis (SLED)

Age-race[a]-sex[b]	Inotropes/PPV[c]	Diagnosis	Outcome[d]
72-B-M	+/+	Myocardial infarction; urosepsis; prostate cancer	D
39-B-F	+/+	Sepsis; disseminated head and neck cancer	D
55-W-M	+/+	Sepsis; MM[e]; s/p BMT[f]	A
32-W-F	+/+	End-stage CHF[g]; s/p CABG[h] +MVR[i]	D
87-W-M	+/+	Sepsis; MM; s/p chemotherapy	A
41-B-F	+/+	Multitrauma	D
43-B-M	+/+	End-stage CHF; s/p cardiac arrest	A
40-B-F	−/−	Fulminant hepatic failure; MM; ESRD	A
66-W-M	+/+	Sepsis; disseminated lung cancer	D
74-W-M	+/+	Pancreatitis; pneumonia	D
65-W-M	+/+	Sepsis; colonic infarction; infected aortic prosthesis	D
72-B-F	+/+	Sepsis; pneumonia	A
45-W-M	+/+	Sepsis; end-stage liver disease; rhabdomyolysis	A
50-W-M	+/+	Sepsis; end-stage CHF; MM	D
55-B-F	+/−	Sepsis; ESRD	A
74-W-F	+/−	Sepsis; MM; s/p chemotherapy	A
82-W-F	+/+	Sepsis; colonic perforation; ESRD	D
79-W-F	+/+	Sepsis; colonic perforation	A
46-B-M	+/+	Sepsis; bacterial endocarditis; severe burns	D
71-W-M	+/+	Sepsis; MM; s/p BMT	D
60-W-M	+/+	Sepsis; disseminated lung cancer	A
80-W-M	+/+	Sepsis; s/p CABG	D
59-W-M	+/+	Sepsis; end-stage liver disease	D
70-W-M	+/+	Sepsis; colonic infarction; s/p CABG + MVR	D
61-W-M	+/+	Ehrlichiosis; rhabdomyolysis	A
57-W-M	+/+	Sepsis; MM; s/p BMT	D
71-W-M	+/+	Sepsis; MM; s/p BMT	A
25-W-M	+/+	Vasulitis; rhabdomyolysis	A
78-W-M	+/+	Sepsis; s/p CABG + MVR	D
83-W-M	+/+	End-stage CHF	D
47-W-F	+/+	End-stage CHF; MM; ESRD	A
31-W-F	+/+	Sepsis; MM; s/p chemotherapy	D
35-W-F	+/+	Sepsis; MM; s/p BMT	D
52-B-M	+/+	Sepsis; MM; s/p chemotherapy	D
58-B-M	+/+	Sepsis; end-stage liver disease	D
71-W-M	+/+	Sepsis; colonic perforation; myocardial infarction	D
56-W-M	+/+	Sepsis; end-stage CHF; s/p CABG +MVR	D

[a] Results are given as B (black), H (Hispanic), W (white)
[b] Results are given as M (male), F (female)
[c] Positive pressure ventilation (PPV)
[d] Results are given as A (alive at hospital discharge), D (dead during hospitalization)
[e] Multiple myeloma (MM)
[f] Bone marrow transplant (BMT)
[g] Congestive heart failure (CHF)
[h] Coronary artery bypass grafting (CABG)
[i] Mitral valve replacement (MVR)

output was 234.8 ± 368.8 (3 to 1748) mL/day. Of 145 SLED treatments, 117 were performed for patients receiving concurrently administered nutrition (47% intravenous, 30% enteral, and 4% combined).

In two patients, the indication for SLED was failure of solute control despite daily IHD. In 35 patients, the indication for SLED was hemodynamic intolerance to IHD, despite the ubiquitous use of inotropic agents and resuscitative intravenous fluids. Of this latter group, 23 patients failed a trial of IHD, whereas in the remainder IHD had been withheld because of clinician determination that hemodynamic intolerance was likely. Table 2 compares hemodynamic profiles, inotropic agent requirements, and illness severity scores between the patients with actual versus anticipated failure of IHD.

The observed hospital mortality was 62.2%. The capacity of the APACHE II model to predict hospital mortality in the SLED patient cohort is graphically displayed in Figures 1 and 2. Goodness-of-fit statistics are associated with high *P* values (suggesting a good fit). Hospital mortality ratios are provided in Table 3 and indicate that the number of observed hospital deaths was not significantly different from that expected from the APACHE II scores.

SLED characteristics

A total of 145 SLED treatments were performed. The median number of SLED treatments per patient was two (range 1 to 30, mean ± SD, 3.9 ± 6.1). The median number of patient days during which SLED was performed without interruption by IHD was two (range 1 to 66, mean ± SD, 7.5 ± 14.1). Prescribed blood flow

Table 2. Actual versus anticipated intermittent hemodialysis (IHD) patients

Parameter	Actual	Anticipated
Number of patients[a]	23	12
Pre-SLED MAP	72.5 ± 16.3 (40.7–112.0)	67.6 ± 9.3 (49.0–86.0)
Pre-SLED pulse	100.2 ± 18.7 (68.0–154.0)	97.8 ± 19.6 (70.0–127.0)
Inotrope number at first SLED[c]	0.9 ± 1.0 (0.0–4.0)	2.0 ± 0.9 (1.0–3.0)
Organs failed (ICU admission)	4.5 ± 1.4 (1.0–7.0)	5.0 ± 1.3 (2.0–6.0)
Organs failed (dialytic initiation)	5.3 ± 1.3 (3.0–7.0)	6.0 ± 0.9 (5.0–7.0)
APACHE II score (ICU admission)	27.8 ± 8.2 (12.0–55.0)	31.8 ± 11.7 (11.0–46.0)
APACHE II expected mortality (ICU admission)	62.6 ± 21.4 (15.0–99.0)	70.2 ± 28.8 (14.0–96.0)
APACHE II score (dialytic initiation)[b]	30.1 ± 8.2 (19.0–52.0)	35.7 ± 7.6 (21.0–45.0)
APACHE II expected mortality (dialytic initiation)[b]	68.8 ± 23.6 (19.0–99.0)	82.7 ± 16.7 (42.0–97.0)

Results are given as mean ± SD (range).
[a] The indication for SLED was hemodynamic instability in 35 patients
[b] $P < 0.05$ actual vs. anticipated Student t test (two-tailed)

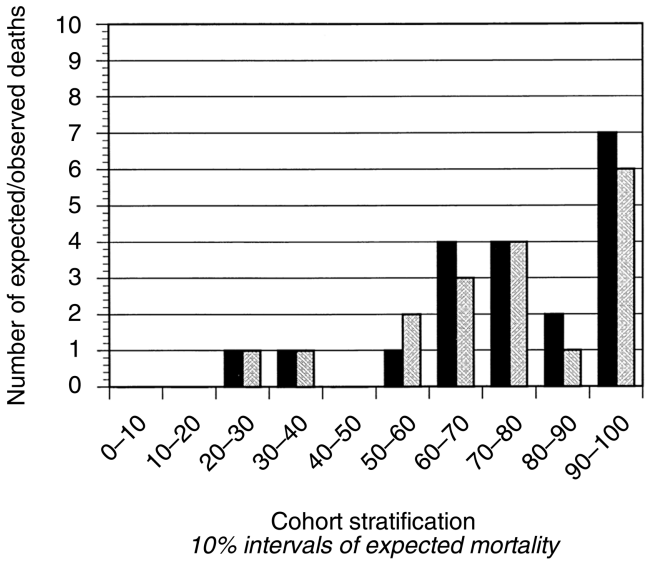

Fig. 1. Patient outcome prediction by APACHE II score at admission to intensive care unit (ICU). Expected (■) versus observed (▩) hospital deaths for 37 patients treated with sustained low-efficiency dialysis (SLED) from July 1998 to January 2000 ($\chi^2 = 1.54$, $P = 0.96$).

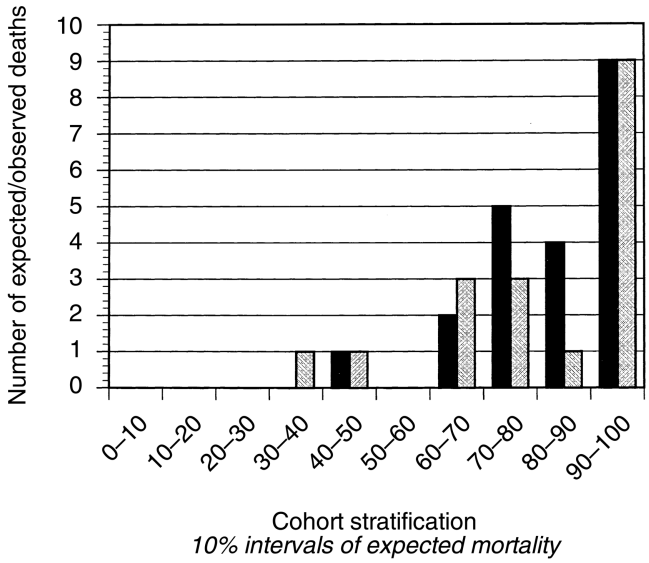

Fig. 2. Patient outcome prediction by APACHE II score at the initiation of dialysis in the ICU. Expected (■) versus observed (▩) hospital deaths for 37 patients treated with SLED from July 1998 to January 2000 ($\chi^2 = 6.1$, $P = 0.53$).

rate was 201.1 ± 7.5 (200 to 250) mL/min, and all treatments were performed with dialysate flow at 100 mL/min. Dialysate potassium concentrations varied from 2 (2% of treatments) to 4 (62% of treatments) mEq/L, and calcium concentrations varied from 1.7 (1% of treatments) to 3.0 (5% of treatments) mEq/L, with the majority being 2.5 mEq/L.

Fifty-one (34.5%) SLED treatments were prematurely discontinued. Twenty-nine (20%) were discontinued for extracorporeal blood circuit clotting and 11 (7.6%) for intractable hypotension. The remaining treatments were discontinued for miscellaneous problems, which included RO leak, machine or angioaccess failure, arrhythmia, withdrawal of therapy, massive gastrointestinal bleeding, emergent surgery, and death secondary to acute pericardial tamponade. The overall SLED treatment duration was 10.41 ± 2.73 (0.5 to 12) hours and 7.56 ± 2.88 (0.5 to 11.75) hours for the 51 prematurely discontinued treatments.

Hemodynamic stability

Mean arterial pressure (MAP) pre-SLED was 69.1 ± 13.8 (40.7 to 119.7) mm Hg, and post-SLED was 68.9 ± 16.7 (39.0 to 113.0, $P = 0.26$) mm Hg. Pulse pre-SLED was 99.0 ± 15.6 (63.0 to 154.0) per minute, and post-SLED was 101.2 ± 16.4 (59.0 to 157.0). This increase in pulse during SLED of 2.2 ± 11.5 per minute was statistically significant ($P < 0.05$). Core temperature pre-SLED was 37.0°C ± 0.7°C (34.3°C to 38.8°C), and post-SLED was 37.0°C ± 0.6°C (35.0°C to 38.8°C, $P = 0.17$).

Inotropic agents were concurrently administered during 27 of the 35 treatments where SLED was performed for the first time in patients who had previously been hemodynamically intolerant to IHD. Eighty of the over-

Table 3. Expected outcomes of patients treated with SLED

	Expected hospital mortality %[a]	Hospital mortality ratio[b]
APACHE II (ICU admission)	66.3 ± 25.6 (14.0–99.0)	0.92 (0.78–1.22)
APACHE II (dialytic initiation)	74.1 ± 23.1 (19.0–99.0)	0.83 (0.70–1.00)

Thirty-seven patients were treated with SLED between July 1998 and January 2000.
[a] Results are given as mean ± SD (range)
[b] Results are given as parameter (95% confidence intervals)

all 145 SLED treatments were in patients receiving inotropic agents. The median number of concurrently administered inotropic agents per patient pre-SLED was one (range 1 to 4, mean ± SD, 1.4 ± 0.7), and this did not change significantly post-SLED (median 1, range 1 to 3, mean ±, SD 1.4 ± 0.7). However, half of the inotropically supported patients underwent an increase in inotrope dose (median 66.7%, range 0 to 500%, mean ± SD, 98 ± 105.5%), and three treatments required an additional inotropic agent for hemodynamic stability.

Twenty-five SLED treatments were associated with one or more episodes of hypotension (defined as the need for resuscitative intravenous fluids >250 mL per treatment and/or modification of ultrafiltration goals). The problem was insurmountable in 11 of these treatments, leading to premature discontinuation of SLED. Post-SLED MAP in these treatments was 48.9 ± 7.4 (39 to 61) mm Hg.

Prescribed ultrafiltration per treatment was 3.0 ± 1.4 (0 to 6) L. The achieved ultrafiltration per treatment was 2.8 ± 1.5 (0 to 6) L after correction for the treatments was abandoned because of extracorporeal blood circuit clotting, machine failure, and other miscellaneous causes.

Small solute clearances

Nine oligoanuric (urine output <150 mL/24 h) patients underwent total dialysate collection, and all successfully completed their prescribed SLED treatments. Total dialysate urea nitrogen removal was 28.6 ± 10.9 (12.7 to 43.8) g per treatment, and double-pool Kt/V was 1.36 ± 0.38 (0.86 to 2.08). Dialysate phosphate removal was 1.5 ± 0.6 (0.8 to 2.5) g per treatment. Of the total urea nitrogen and phosphate removal, 24.4 ± 2.6% (20.6 to 27.0%) and 26.9 ± 2.6% (22.5 to 34.4%), respectively, occurred in the last four hours of SLED treatment.

Comparisons of pre- and post-SLED solutes are shown in Table 4. Significant changes were seen in potassium, creatinine, blood urea nitrogen, venous bicarbonate, phosphate, and total calcium. Hypokalemia in the 12 hours following SLED was noted in seven treatments, requiring supplementation of 41.4 ± 14.6 (20 to 60) mEq. Similarly, 18 SLED treatments resulted in PO_4 supplementation of 21.3 ± 7.5 (10 to 40) mmol.

Anticoagulation

Forty-one SLED treatments were performed without anticoagulation. Of the remaining 104 treatments, 8 were performed in patients already anticoagulated for other indications. In these cases, a decision was made to defer the prescription of additional anticoagulant with SLED. The remaining 96 treatments were performed with concurrently administered unfractionated heparin. An extracorporeal circuit infusion at a rate of 481.1 ± 290.5 (100 to 1400) IU/h was used for all of these treatments, whereas a loading dose [1884.6 ± 1431.1 (1000 to 6000) IU] was given at SLED initiation only for 13 treatments. During heparinized treatments, the maximum recorded APTT was 52.3 ± 30.4 sec (13.7 to 120 sec) as compared with the immediate pre-SLED APTT of 47.0 ± 22.0 sec (22.1 to 120 sec) in the heparin-free group ($P = 0.29$).

Extracorporeal blood-circuit clotting occurred in 38 SLED treatments. Nine of these 38 treatments were reinitiated, and the rest were discontinued at the discretion of the nephrologist. Neither the administration of heparin with SLED [odds ratio 0.80 (95% CI, 0.53 to 1.21)] nor anticoagulation by other means [odds ratio 0.83 (95% CI, 0.56 to 1.23)] was statistically associated with a lower probability of circuit clotting. APTTs, international normalized ratios (INRs), and platelet counts were not significantly different between SLED treatments that clotted and those that did not.

Bleeding complicated 2 out of 145 SLED treatments. The first episode (hemorrhagic pericardial tamponade within 48 hours of coronary artery bypass grafting) occurred in the absence of any anticoagulant, while the second (massive hemorrhage from multiple previously unrecognized upper gastrointestinal ulcers) occurred six hours after heparinization specifically for SLED.

DISCUSSION

A total of 145 SLED treatments were performed in 37 patients over the 18-month study period. The patients were critically ill, with expected hospital mortality rates that were similar to those previously reported for patients with multiorgan failure undergoing CRRTs [10, 27]. All had either failed IHD or were justifiably anticipated to do so. In general, SLED was a safe, effective, and convenient renal replacement therapy in these patients.

There is concern that hypotension during renal replacement therapy may be detrimental to renal recovery (abstract; Manns et al, *ASAIO J* 42:78, 1996) [28]. Many retrospective studies have suggested that CRRTs are

Table 4. Solute changes pre- and post-SLED in 9 patients undergoing completed SLED treatments

Solute	Pre-SLED	Post-SLED *60 min*	*P* value
Sodium *mEq/L*	137.6 ± 4.1 (129–143)	136.7 ± 3.4 (131–142)	0.5
Potassium *mEq/L*	4.6 ± 0.8 (3.4–5.7)	3.9 ± 0.5 (3.4–4.5)	0.02
Venous bicarbonate *mEq/L*	20.3 ± 6.5 (7–28)	24.4 ± 3.2 (18–28)	0.02
BUN *mg/dL*	71.6 ± 25.5 (30–109)	31.0 ± 11.5 (16–47)	0.0001
Creatinine *mg/dL*	3.4 ± 2.0 (1.7–8.2)	1.6 ± 0.8 (0.8–3.5)	0.003
Total calcium *mg/dL*	7.9 ± 1.2 (5.7–9.8)	8.7 ± 1.4 (7.0–10.8)	0.005
Phosphate *mg/dL*	5.9 ± 2.1 (3.5–9.5)	3.4 ± 1.0 (2.3–5.0)	0.0003
Albumin *g/dL*	2.2 ± 1.1 (1.0–3.5)	2.3 ± 1.3 (1.0–3.9)	0.8

Results are given as mean ± SD (range); *P* values are by the paired Student *t* test (one-tailed).

superior to IHD in terms of hemodynamic stability (abstract; Manns et al, *J Am Soc Nephrol* 6: 470, 1995) [3, 10–12], and a single prospective study in dispute of this has been criticized for methodological flaws [29]. However, it is clear that hemodynamic instability can still occur with hemofiltration if fluid removal is too large or rapid, and previous investigators have reported higher rates of hypotension with intermittent rather than continuous hemofiltration [30]. SLED was hemodynamically tolerated in most patients, and precise achievement of ultrafiltration goals was possible in most cases. However, hypotension did occur during several SLED treatments and necessitated SLED discontinuation in 7.6% of treatments. Patients on inotropic agents often needed an increase in dose for hemodynamic support during SLED, and this may have contributed to cardiac dysrhythmia in one patient. However, these findings must be considered in the context that these patients had already demonstrated intolerance to IHD. Three of the 11 patients who were persistently hypotensive with SLED were subsequently treated with continuous venovenous hemofiltration (CVVH), and all were hemodynamically intolerant to this therapy as well. Conceivably, hemodynamic stability during SLED may be improved by lengthening the treatment duration, although in our experience, hypotension that did not necessitate the discontinuation of SLED was easily treated, and increases in inotropic support only transient. Since treatment failure with SLED due to hypotension was predictive of failure with CVVH, we do not plan to change our duration of SLED protocol. However, if in individual patients increasing the SLED duration is helpful, we would recommend that application.

Complications associated with SLED were common to all CRRTs. Extracorporeal blood circuit clotting occurred in approximately 25% of SLED treatments prior to completion. For CRRTs, APTT is a good predictor of filter clotting [31], and most opinion leaders recommend an APTT of 10 to 20 seconds above control [31, 32]. The high incidence of thrombocytopenia in our group (47% of patients with platelet counts less than 100,000/mm^3 at SLED initiation) was a factor in the conservative approach to anticoagulation. Heparin-free SLED was performed in approximately 30% of cases. Heparin administration in the remaining treatments usually consisted of an extracorporeal circuit infusion without an initial loading dose. The percentage of heparin-free dialysis in our series is higher than has been reported with CRRTs [33], and it is conceivable that a more aggressive anticoagulation protocol could have resulted in less clotting, but possibly more bleeding complications.

Sustained low-efficiency dialysis provided adequate small solute clearances and an acceptable dialysis dose. The ability for SLED to provide adequate clearances despite low blood flow rates makes it an appealing option for patients with marginally functional temporary accesses. SLED prescription could be varied in clinical situations to suit the goals for clearance on an individual basis. Serious electrolyte disturbances did not occur, but some patients needed phosphate and potassium supplementation. Electrolytes need to be closely monitored, especially if SLED is performed on a daily basis.

For both traditional CRRTs and SLED, responsibilities are shared between ICU and dialysis nurses, and the success of such programs is critically dependent on the skills and training of ICU nurses [5]. SLED has been well accepted by ICU nursing staff and is simpler than CVVH to manage at a nursing level (abstract; Hall et al, *Blood Purif* 17:36, 1999). Because of the decreased nursing workload, the patient to ICU nurse ratio is 2:1 for SLED compared with the 1:1 ratio often required for CRRTs. The transition to nocturnal scheduling has been successful and is convenient in allowing unrestricted patient access for daytime procedures and tests. Furthermore, at UAMS the same 2008H equipment has been used for conventional IHD during the day and then SLED at night. The use of the 2008H for SLED allows for considerable savings in an initial equipment investment when compared with traditional CRRTs. A program of SLED is also less expensive to maintain than traditional CRRTs, regardless of machinery or replacement solutions utilized (abstract; Alam et al, *Am J Kidney Dis* 35:A9, 2000). In previous reports, considerable modifications have been necessary to enable existing hemodialysis machines to provide CRRT [34], while in our current pro-

gram, the new CRRT software allows the 2008H to be quickly adapted between SLED and IHD.

The duration of dialysis treatments may have a positive impact on survival in critically ill patients with ARF, and SLED could have a role in the treatment of such patients irrespective of their hemodynamic stability. Prospective studies directly comparing SLED to traditional CRRTs will help define the exact role for SLED in the critical care setting, although a leading indication would be in acute dialysis programs where traditional CRRTs are unavailable. In conclusion, our recent experience suggests that SLED is a viable alternative to traditional CRRTs as renal replacement in critically ill patients in whom IHD had previously failed or been withheld.

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APPENDIX

Total urea removal (U) was determined by total dialysate collection. The following equations have been derived previously [26] and are generated under the conditions of a variable-volume, double-pool urea kinetic model and $K_R = 0$. Urea equilibrium was assumed at 60 minutes post-SLED. Serum blood urea nitrogen (BUN) was divided by 0.93 for conversion to plasma urea nitrogen (PUN). Double-pool V were calculated from urea mass balance:

Double-pool V

$$= \frac{U - PUN_{pre} \times (BW_{pre} - BS_{post}) - PUN_{next} \times \frac{T + 60}{\Phi - 60} \times (BW_{next} - BW_{post})}{PUN_{pre} - PUN_{equil} + \frac{T + 60}{\Phi - 60} \times (PUN_{next} - PUN_{equil})}$$

where T, Φ, and BW refer to intradialytic time, interdialytic time, and body weight, respectively, and the subscripts of pre, post, equil, and next refer to pre-SLED values, post-SLED values, values 60 minutes post-SLED, and values at the start of the following dialysis treatment respectively. Double-pool G were calculated from classical UKM as proposed by Gotch et al:

Double-pool G

$$= \frac{PUN_{next} \times (\text{Double-pool V} + BW_{next} - BW_{post}) - PUN_{equil} \times \text{Double-pool V}}{\Phi - 60}$$

Double-pool K were estimated:

$$\text{Double-pool K} = \frac{U}{T + 60} \times \frac{\ln\left(\frac{PUN_{pre}}{PUN_{equil}}\right)}{(PUN_{equil} - PUN_{pre})}$$

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